OVERVIEW OF BUTYLATE RISK ASSESSMENT

Introduction

This document summarizes EPA's human health findings and conclusions for the thiocarbamate pesticide butylate, as presented fully in the documents: *Butylate-HED Revised Human Health Assessment, February 26, 2001*; and: *GENEEC and SCI-GROW2 EEC's for the Current Use of Butylate on Corn for the Purpose of Tolerance Reassessment, August 20, 1998*. The purpose of this summary is to assist the reader by identifying the key features and findings of this risk reassessment in order to better understand the conclusions reached in the tolerance reassessment. This summary was developed in response to comments and requests from the public, which indicated that the risk assessments (and other like documents) were difficult to understand, that they were too lengthy, and that it was not easy to compare the assessments for different chemicals due to the use of different formats.

The Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act (FQPA) of 1996, requires EPA to review all the tolerances for registered chemicals in effect on or before the date of the enactment of FQPA. In reviewing these tolerances, the Agency must consider, among other things, aggregate risks from non-occupational sources of pesticide exposure, whether there is increased susceptibility to infants and children, and the cumulative effects of pesticides with a common mechanism of toxicity. The tolerances are considered reassessed once the safety finding has been made or a revocation occurs. A reregistration eligibility decision (RED) for butylate was completed in September 1993, prior to FQPA enactment; therefore it needed to be updated to consider the provisions of the Act.

FFDCA, as amended, requires that the Agency, when considering whether to establish, modify, or revoke a tolerance, consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The Agency is currently examining whether and to what extent thiocarbamates pesticides may share a common mechanism of toxicity. Preliminary determinations indicate that the potential to produce a common toxic effect, neuropathy (e.g., degeneration and demylination of the sciatic nerve), and the similarities in structure and metabolism, may support grouping of the thiocarbamates based on their ability to produce a common effect by a common mechanism. Assuming these assertions are correct, preliminary screening-level chronic cumulative dietary food risk analyses do not provide evidence that cumulative exposure of the human population, including infants and children, to the neuropathic thiocarbamates would raise concern of adversely affecting human health.

The preliminary determination of whether and to what extent thiocarbamates pesticides may share a common mechanism of toxicity, and accompanying screening-level cumulative dietary

analyses are to be presented to the FIFRA Science Advisory Panel for peer review on September 7, 2001. Pending their review of the information, the Agency expects to complete the cumulative risk assessment for thiocarbamate pesticides, at which time, provided the risk analyses concludes chronic cumulative dietary risks are not of concern to the Agency, the butylate tolerances will be considered reassessed, in accordance with FFDCA, as amended.

The risk assessment, and documents pertaining to the Agency's report on FQPA tolerance reassessment progress and interim risk management decision for butylate are available on the Internet at http://www.epa.gov/pesticides/reregistration/status.htm and the public docket for viewing. Because the dietary risks posed by the use of butylate are low and not of concern to the Agency, the normal process of meeting stakeholders (i.e., growers, extension offices, commodity groups, and other government offices) to discuss the identified risks and solicit input on risk mitigation strategies is not necessary for this chemical. Rather, the Agency's report on FQPA tolerance reassessment progress and interim risk management decision for butylate will be announced in the Federal Register. Since there are no risk concerns for butylate alone, no further actions are warranted t this time, pending a determination of whether a full reassessment of the cumulative risk from thiocarbamate pesticides, such as butylate, may be needed and is completed.

Use Profile

Herbicide: Butylate is a soil incorporated selective herbicide registered solely for use on corn (field, sweet and popcorn) for control of grassy and broadleaf weeds and nutsedge. Typically targeted weeds include nutsedge, seedling johnsongrass, goosegrass, crabgrass, barnyard grass, and a variety of foxtail (giant, green, and yellow). There are no registered non-food/non-feed uses, and no existing or proposed residential uses of butylate products.

Formulations: Formulated as a liquid emulsifiable concentrate (85.1% active ingredient).

Methods of Application: Butylate may be applied preplant, at plant, postplant, and after harvest (fall) to corn, popcorn, and sweet corn at a maximum single and annual application rate of 6.3 pounds of active ingredient per acre (lbs a.i./A). Butylate is a highly volatile; consequently, applications with butylate are made by ground equipment, either broadcast or band, and are immediately incorporated into the soil. The type of equipment used to apply butylate include, boom sprayer; soil injection equipment; and center pivot irrigation.

Use Summary: Usage of butylate has declined from approximately 15 million lbs a.i. in 1991 to an estimated 950,000 lbs a.i. in 1998. The estimated annual production of butylate from 1993 to 1997 average is approximately 1 million lbs a.i. Butylate was not produced in 1998 and usage and production are expected to continue to decline. Table 1 illustrates the estimated usage of butylate.

Registrant: TRI AG, Inc.

Table 1. Butylate Usage

Crop	Acres Grown (000)	Acres Treated (000)		% Crop Treated		Lbs A.I. Applied (000)		States of Most Usage (% of lbs a.i. Used)
		Avg	Max	Avg	Max	Avg	Max	
Sweet Corn	784	17	35	2	4.5	50	101	FL WI NY NJ CA GA (79%)
Corn[1]	71,264	375	1,032	.5	1.4	900	2,477	IN IL KY NE MO KS (64%)
Total	72,048	392	1,067			950	2,578	

COLUMN HEADINGS
Avg = Weighted average in which the most recent years and more reliable data are weighted more heavily.
Max = Estimated maximum, which is estimated from available data.
[1] Includes field corn and popcorn

Human Health Risk Assessment

Acute Dietary (Food) Risk

Acute dietary risk from food is calculated considering what is eaten in one day (in this instance, the full range of consumption values as well as the range of residue values in food). A risk estimate that is less than 100% of the acute Population Adjusted Dose (aPAD) (the dose at which an individual could be exposed on any given day and no adverse health effects would be expected) is not of concern to the Agency. The aPAD is the reference dose (RfD) adjusted for the FQPA Safety Factor. A deterministic Tier I analysis at the 95th percentile using tolerance level residues and 100 % crop treated (%CT) was conducted to assess acute dietary (food) risk for butylate. Table 2 presents the results of the acute dietary (food) exposure and risk analysis.

Table 2. Acute Dietary (Food) Exposure and Risk

Population Subgroup	Exposure (mg/kg/day)	% aPAD
General U.S.	0.000377	<1

Population Subgroup	Exposure (mg/kg/day)	% aPAD
Females (13-50 years)	0.000309	<1
All infants	0.000645	<1
Children (1-6 years)	0.000768	<1

- For the general population, the acute No Observed Adverse Effects Level (NOAEL) of 600 mg/kg/day was established, based on clinical signs and acute neurotoxic effects (i.e., neuronal cell necrosis in the brain and degeneration of sciatic nerve), which were seen only at the highest dose tested in the acute rat neurotoxicity study (also the Lowest Observed Adverse Effects Level (LOAEL)) of 2000 mg/kg/day.

- For the females (13-50 years) population subgroup, the acute NOAEL of 40 mg/kg/day was established, based on decreased fetal weights and increased incidences of misaligned sterebrae in the rat developmental study at the LOAEL of 400 mg/kg/day. In this study, both maternal and developmental toxicity were observed at the same dose (400 mg/kg/day); therefore, no increased susceptibility to offspring was observed.

- An uncertainty factor of 100 was applied to account for inter-species extrapolation (10 X) and intra-species variability (10 X).

- FQPA safety factor was removed (reduced to 1 X) since: the toxicology data base is complete; the developmental and reproductive toxicity data did not indicate increased sensitivity or susceptibility of rats or rabbits to *in utero* and/or postnatal exposure; unrefined dietary exposure estimates (assuming all commodities contain tolerance level residues) will overestimate dietary exposure; modeling data are used for ground and surface source drinking water exposure assessments resulting in estimates considered to be upper-bound concentrations ; and there are currently no registered residential uses for butylate. Additionally, there is no evidence to support a recommendation for a developmental neurotoxicity study.

- Because the FQPA Safety Factor was removed (reduced to 1 X) for acute exposures; the aPAD and the acute RfD are identical at 6 mg/kg/day for the general U.S. population, and 0.4 mg/kg/day for the females (13-50 years) subgroup.

- The acute dietary exposure analysis is based on the Dietary Exposure Evaluation Model (DEEM™). The DEEM™ analysis evaluated the individual food consumption as reported by respondents in the USDA 1989-92 Continuing Surveys for Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity.

- The acute dietary (food) assessment for butylate is a Tier I deterministic analysis at the 95th percentile, and was conducted using tolerance level residues (0.1 ppm) and 100% CT.

The analysis shows that acute dietary (food) exposure and risk for butylate is low (<1% of aPAD) and is not of concern to the Agency.

Chronic Dietary (Food) Risk

Chronic dietary risk from food is calculated by using the average consumption values for food and average residue values for those foods over a 70-year lifetime. A risk estimate that is less than 100% of the chronic PAD (cPAD) (the dose at which an individual could be exposed over the course of a lifetime and no adverse health effects would be expected) is not of concern to the Agency. Table 3 presents the results of the chronic dietary (food) exposure and risk analysis.

Table 3. Chronic Dietary (Food) Exposure an Risk

Population Subgroup	Exposure (mg/kg/day)	% cPAD
General U.S.	0.000150	<1
Females (13-50 years)	0.000110	<1
All infants	0.000310	<1
Children (1-6 years)	0.000353	<1

- The chronic NOAEL of 5 mg/kg/day was established, based on decreased body weight gain (not statistically significant) and increased relative liver weight in male dogs from a 12-month dog feeding study at the LOAEL of 25 mg/kg/day.

- Based on available data, butylate is not carcinogenic, and has been classified as a Group E "not likely" carcinogen; therefore, no chronic (cancer) dietary risk assessment was conducted.

- An uncertainty factor of 100 was applied to account for inter-species extrapolation (10 X) and intra-species variability (10 X).

- As with the acute dietary analysis, the FQPA Safety Factor was removed (reduced to 1 X) for chronic exposures; therefore the cPAD and the chronic RfD are identical at 0.05 mg/kg/day.

- The chronic dietary exposure analysis is based on the Dietary Exposure Evaluation Model (DEEM™). For chronic dietary (food) assessments, a three-day average of consumption for each subpopulation is combined with average residues in commodities to determine average exposures in mg/kg/day.

- Tier I analysis was also conducted for chronic assessments using tolerance level residues and 100% CT. The estimated chronic dietary (food) exposure consumed < 1% of the

cPAD for all population subgroups; therefore, chronic dietary (food) risk is not of concern to the Agency.

Drinking Water Dietary Risk

Drinking water exposure to pesticides can occur through surface and/or ground water contamination. EPA considers acute (one day) and chronic (lifetime) drinking water risks and uses either modeling or actual monitoring data, if available, to estimate those risks. Modeling is carried out in tiers of further refinement, but is designed to provide a high-end estimate of exposure. To determine the maximum allowable contribution from water allowed in the diet, EPA first looks at how much of the overall allowable risk is contributed by food and then determines a "drinking water level of comparison" (DWLOC) to ascertain whether modeled or monitored estimated environmental concentrations (EECs) exceed this level. EECs that are above the corresponding DWLOC are of concern to the Agency.

Based on environmental fate data, butylate is mobile to slightly mobile in soil. However, significant residues of butylate are not expected to reach surface water under most conditions because it is incorporated and partitions from soil to air readily. Even though soil incorporation favors downward movement to ground water over surface runoff, significant ground water contamination is still not expected under most conditions. Since there are no residential risks associated with butylate use, only dietary exposure from food is considered for purposes of calculating the DWLOC.

- Drinking water concentrations were estimated using GENEEC (Tier I-surface water) and SCI-GROW (Tier I-ground water) computer models.

- The drinking water assessment for butylate was conducted on parent butylate only, since no degradates of concern were identified.

- While limited monitoring data from surface and ground water sources are available on butylate and were lower than levels predicted by models, Tier I modeling estimates were used to assess exposure from both surface and ground water sources. These estimates were substantially lower than the DWLOCs and no further refinement was needed. Drinking water DWLOCs and EECs are compared in Table 4.

Table 4. Drinking Water DWLOC and EEC Comparisons

Population Subgroup	DWLOCs (ppb)		EECs (ppb)		
	Acute	Chronic	Ground Water	Surface Water	
				Acute	Chronic
U.S. General	210,000	1745	0.41	33.1	10
Females (13-50 years)	12,000	1497			
All infants	60,000	497			
Children (1-6 years)	60,000	497			

- For **acute** drinking water risk, potential (peak) concentrations of butylate in either surface (33.1 ppb) or ground water (0.41 ppb) result in an exposure that is below the acute DWLOC for females (13-50 years) (1200 ppb), the population subgroup with the highest risk estimate.

- For **chronic** drinking water risk, potential (average) concentrations of butylate in either surface (10 ppb) or ground water (0.41 ppb) results in exposure that is below the chronic DWLOC for infants and children (1-6 years) (497 ppb), the population subgroups with the highest risk estimate.

- Neither GENEEC nor SCI-GROW Tier I drinking water models take into account volatility from soil or water. Because butylate dissipates primarily by volatility from soil, EECs predicted from either model are likely lower.

- Upon comparison of the acute and chronic DWLOCs with the estimated EECs of butylate estimated using conservative modeling, surface and ground water concentrations are substantially lower than the DWLOCs (Table 4) for all populations. Consequently, there is no acute or chronic concern for drinking water from surface or ground water sources.

Residential Risk

Butylate is not registered for home use nor is it used in and around schools, or parks. Thus, there is no residential exposure to assess nor aggregate with the dietary exposure.

Aggregate Risk

Aggregate risk looks at the combined risk from exposure through food, drinking water, and residential uses. Generally, all risks from these exposures must be less than 100% of the aPAD and cPAD. For butylate, the aggregate risks are limited to food and water exposure, because

there are no residential uses.

- Combining both the acute dietary (food) risk estimates with the surface and ground water estimated concentrations (drinking water) for butylate, the acute aggregate (food + drinking water) risk is less than 100% of the aPAD, and therefore, is not of concern to the Agency.

- Combining both the chronic dietary (food) risk estimates with the surface and ground water estimated concentrations (drinking water) for butylate, the chronic aggregate (food + drinking water) risk is less than 100% of the cPAD, and therefore, is not of concern to the Agency.

Occupational and Ecological Risk

Because butylate is under review for tolerance reassessment only, no occupational or ecological risk assessment was conducted for this TRED. Occupational and ecological risk management decisions were made as part of the 1993 Butylate RED and have been implemented.

Tolerance Reassessment Summary

The Agency has sufficient residue data for reassessing the tolerances for butylate uses on corn. Additionally, residues of butylate in or on corn commodities from crop field trials were nondetectable. Because there is no reasonable expectation of finite residues in meat, milk, poultry, and eggs, tolerances for residues of butylate in meat, milk, poultry, and eggs are not required. Based on the residue data submitted, no changes in the current tolerances for butylate are required; therefore, the tolerances remain at 0.1 ppm for all registered commodities, until such time as a determination of whether a full reassessment of the cumulative risk from thiocarbamates pesticides, such as butylate, may be needed and is completed.

Summary of Pending Data

No data are pending at this time.